Nanomanufacturing Summit 2012

& 11th Annual NanoBusiness Conference

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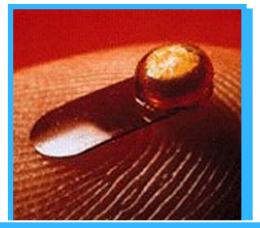
Nanomedicine & Nanodiagnostics

Hong Guo, PhD

pSivida Inc.

Evolution of pSivida's Drug Delivery Systems



1st Generation

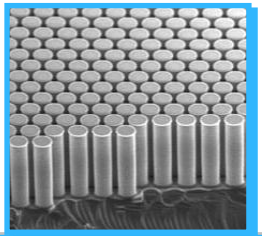
6-9 month duration
FDA approved 1995

2nd Generation

30 month duration
FDA approved 2005

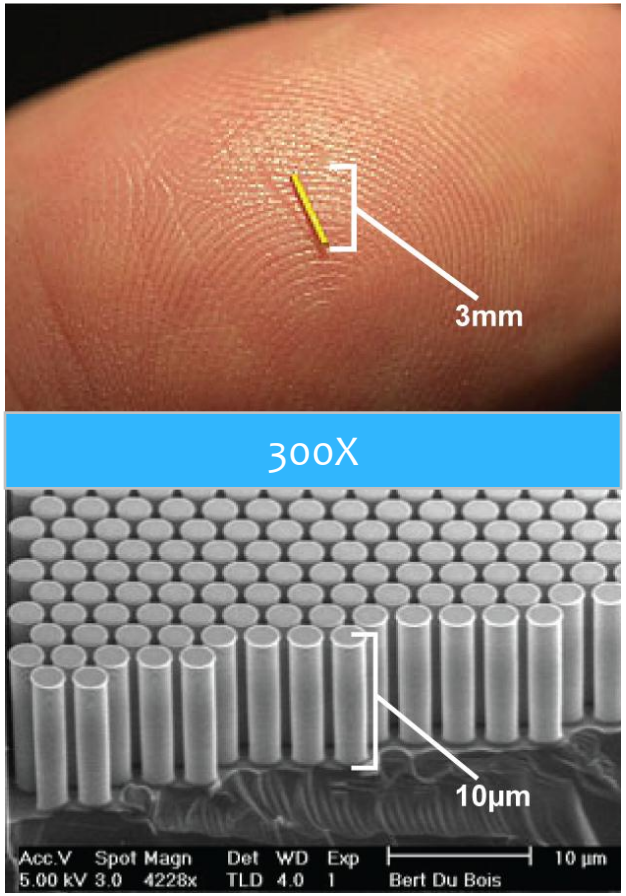
3rd Generation

≤ 30 month duration
Approved in EU 2012



4th Generation

BioSilicon Technology



- Fully bio-erodible
- Potential to deliver drugs, peptides and proteins
- Very promising preliminary data

BioSilicon: A highly porous material

1cm^3 of bioSilicon™
i.e. sugar cube

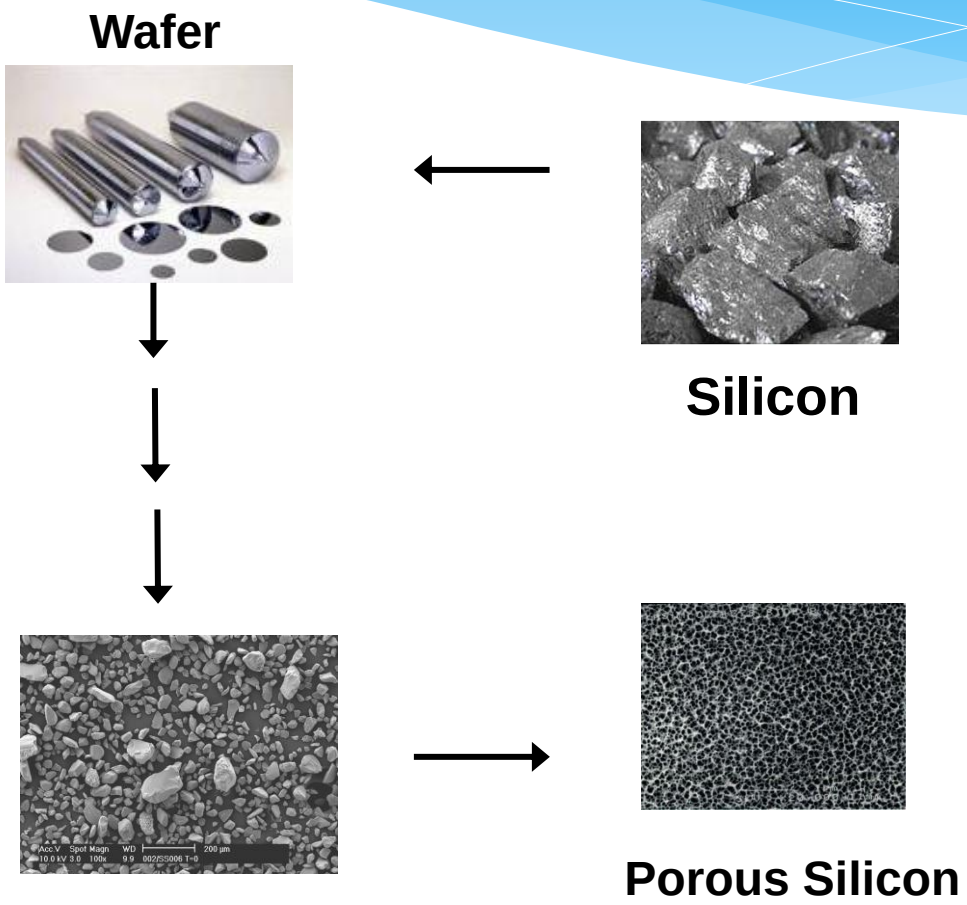
Total surface area equivalent to 2 tennis courts

If the columnar pores were Stacked the length would measure 6 million miles

Porous Silicon

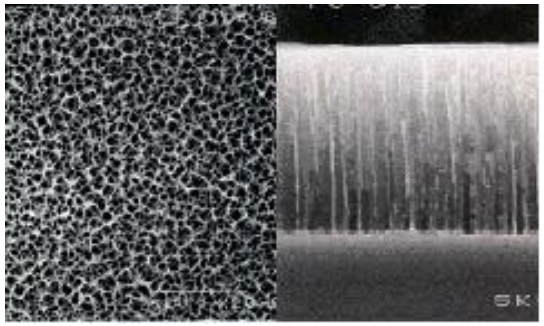
- Manufactured from elemental silicon
- Ultra pure (99.99999%) feedstock
  - Semiconductor grade
- Nano structured and porous
  - Not nanoparticles
- Tunable
  - Micromachinable
  - Pore size, particle size, chemically
- Biodegradable and biocompatible

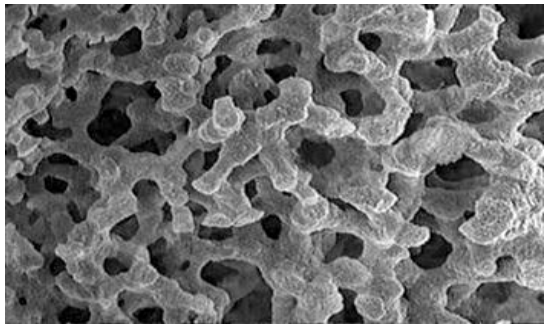
Porosification



Porous Matrices

- Porous Silicon
  - Honeycomb structure
  - Tunable properties
  - Pore size, porosity, oxidation, dissolution
  - Particles
- Silica
  - Interconnected, sponge like structure
  - Agglomeration of primary particles
  - Range of particle and pore sizes



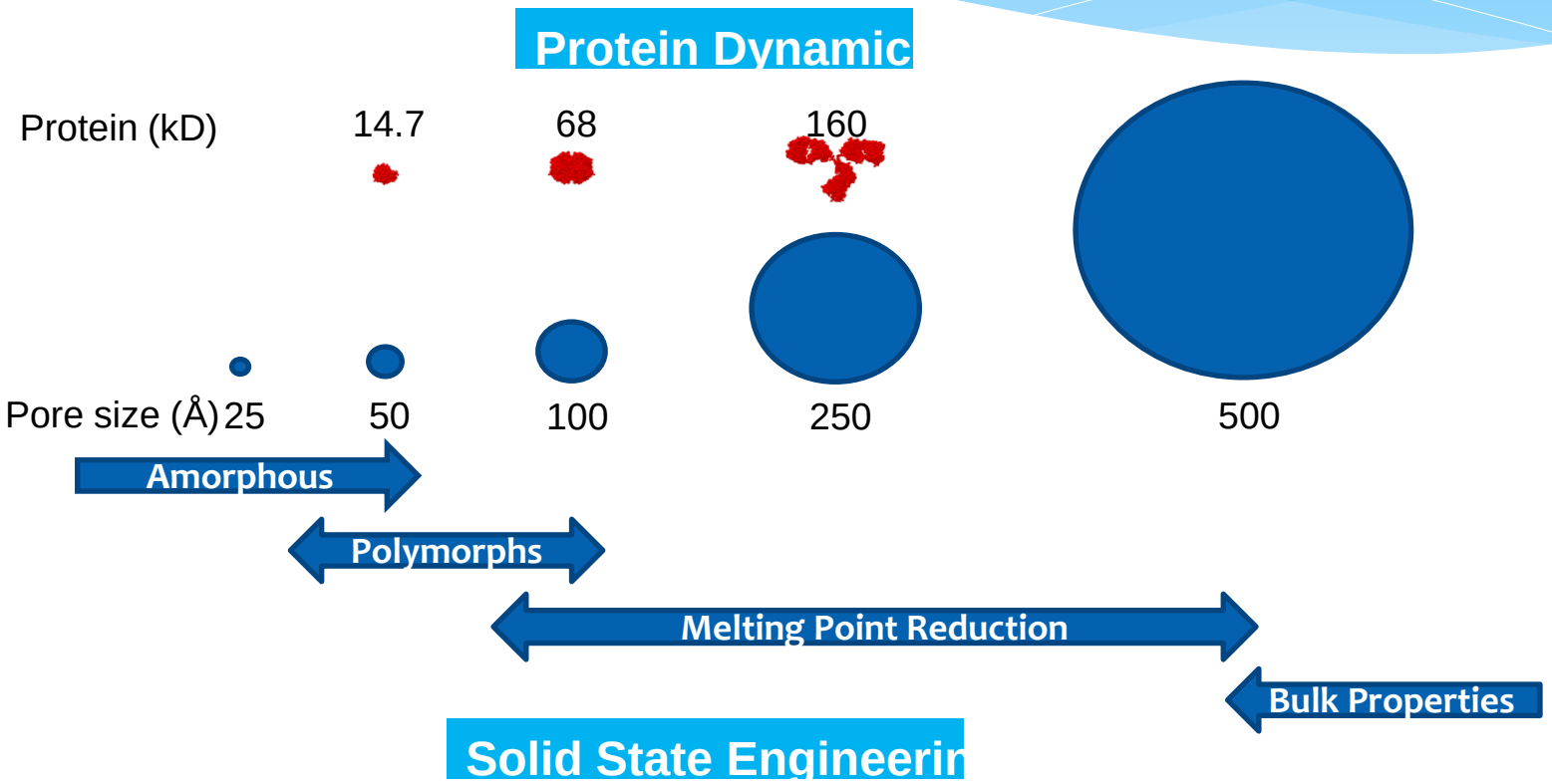


Molecular engineering

- Structural confinement allows crystal engineering
  - Amorphisation
  - Polymorph stabilisation
  - Melting point depression

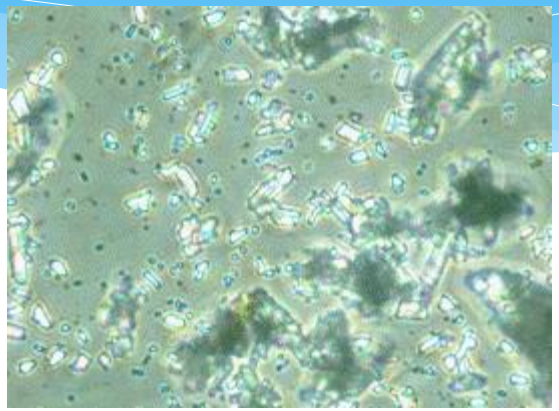
- Controlled nanostructring
  - Pore size, surface area
  - Surface chemistry
  - Selective molecular adsorption and containment

Molecular Engineering

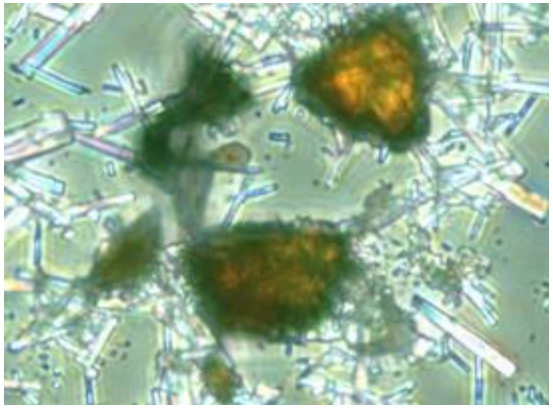


Drug Loaded BioSilicon

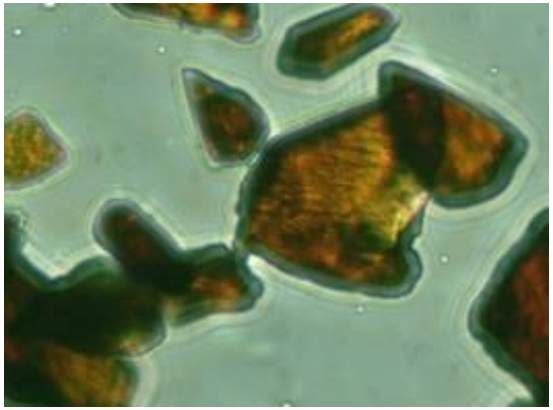
Biosilicon



Unprocessed API



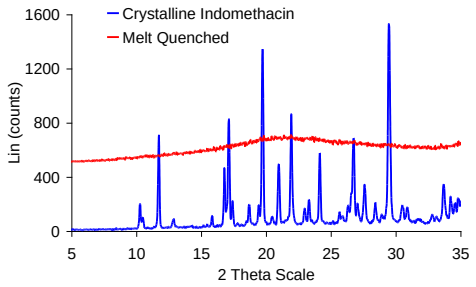
API and Biosilicon



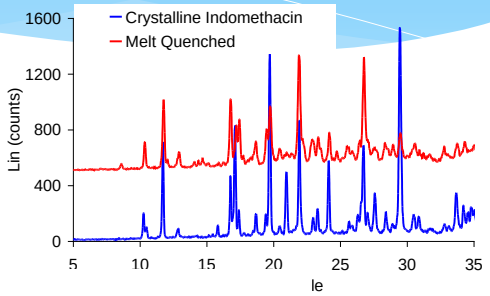
API in Biosilicon

Amorphous Stabilisation

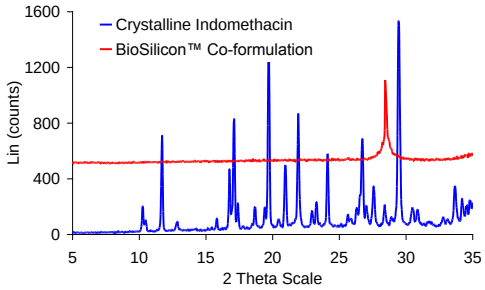
Amorphous control



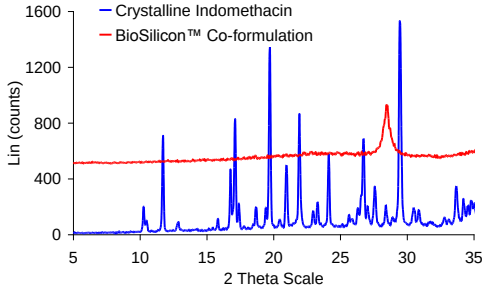
14 days @ 40°C/ 75% RH



Porous silicon co-formulation



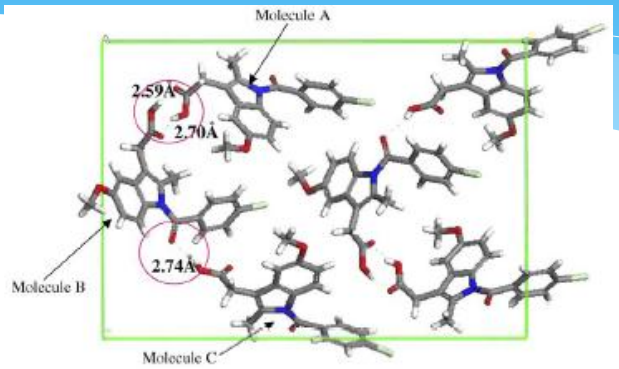
6 month @ 40°C/ 75% RH



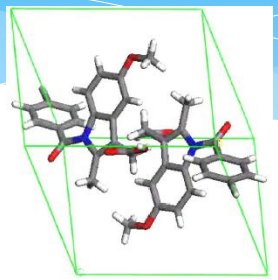
- **Amorphous control recrystallised after 14 days**
- **Porous silicon formulation remained amorphous at 6 months**

Stabilization of Amorophous Form

a=5.4Å
b=25.3Å
c=18.52Å



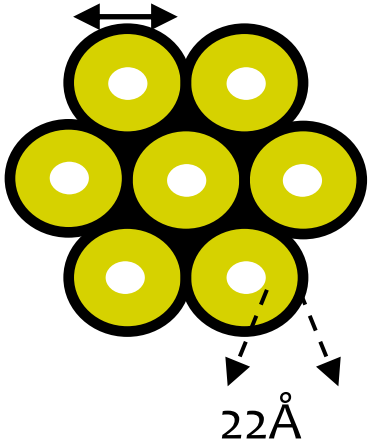
α-polymorph



γ-polymorph

a=9.3Å
b=11.0Å
c=9.7Å

10nm



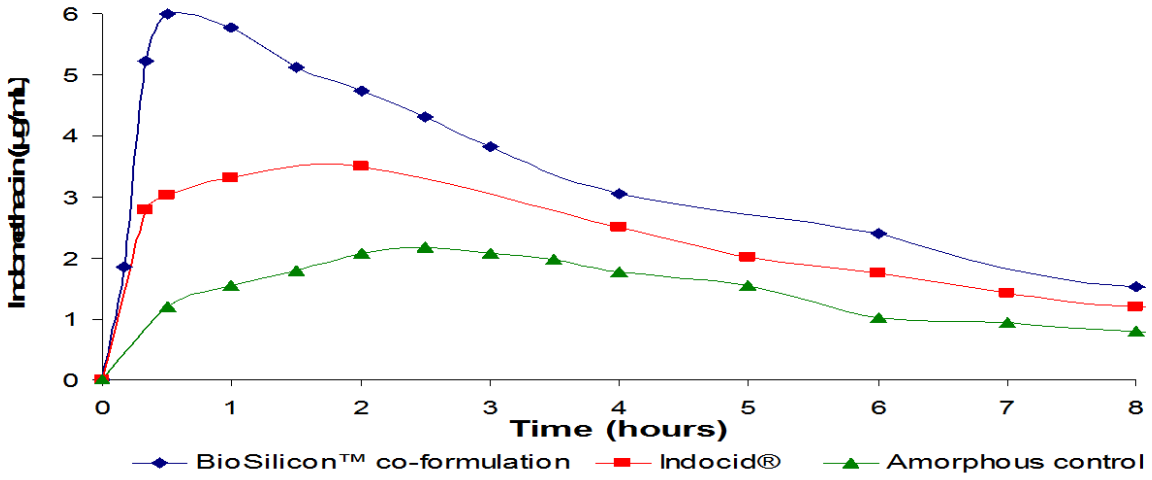
Indomethacin
BioSilicon™

- 20% (w/w) drug loading
- Drug molecule = 4.8Å at longest dimension
- Drug layer = 22Å
- Drug layer is 4 molecules thick
- Insufficient volume to allow recrystallisation
- Physically stabilised amorphous form

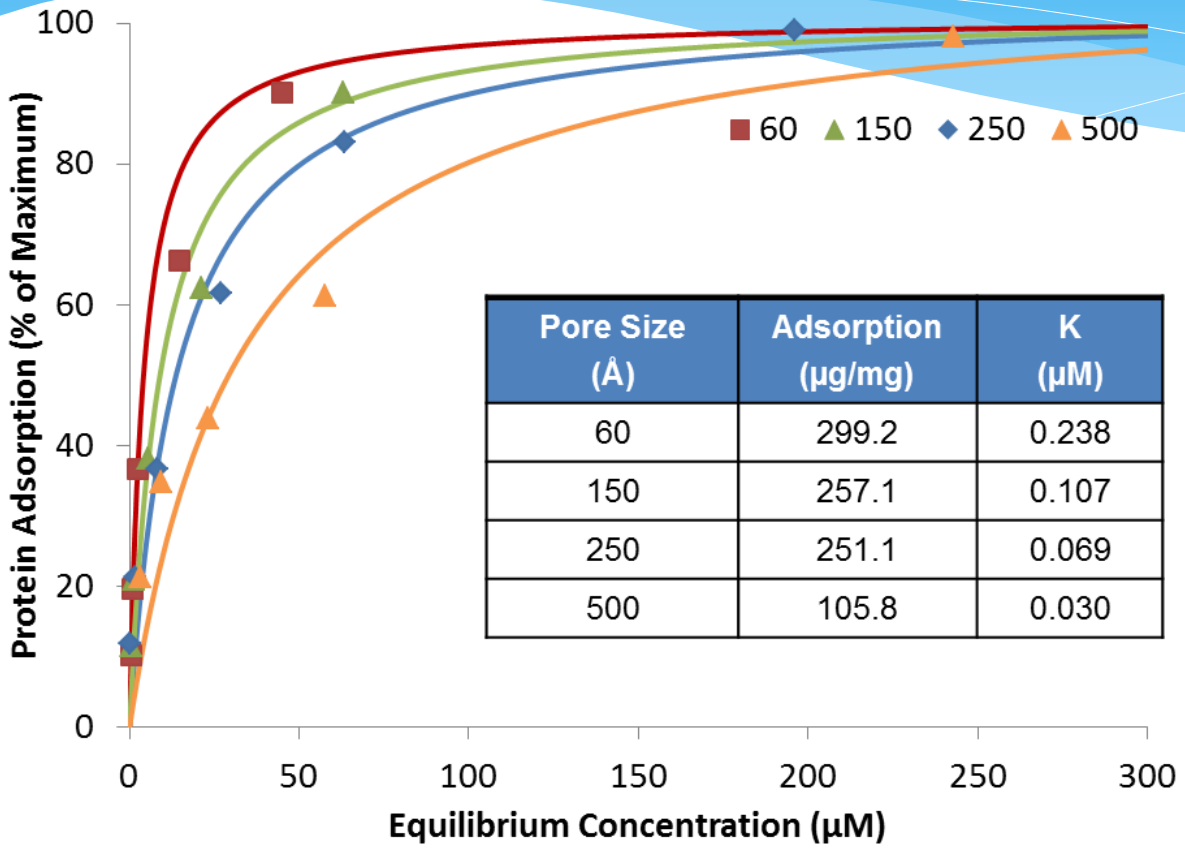
Indomethacin Oral Bioavailability

Pharmacokinetic Parameter		Indomethacin I.V.	Control	BioSilicon Co-formulation	Indocid®
T_{max}	(h)	n/a	2.75 ± 0.65	0.56 ± 0.31	2.00 ± 0.00
C_{max}	(µg/ml)	n/a	2.48 ± 0.38	6.46 ± 0.52	3.49 ± 0.54
$AUC_{0\text{-}24h}$	(h*µg/ml/mg)	66.92 ± 6.73	35.83 ± 1.95	66.98 ± 2.62	51.82 ± 2.33
F (%)	(n/a)	n/a	53.54 ± 2.91	100.1 ± 3.9	77.43 ± 3.49

Sprague-Dawley rates (n=3)

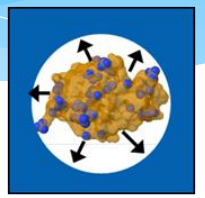


Protein Adsorption

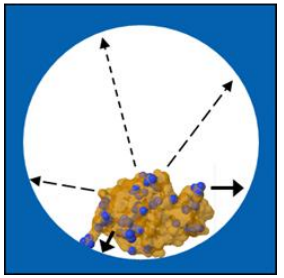


Pore Size (Å)	Adsorption (µg/mg)	K (µM)
60	299.2	0.238
150	257.1	0.107
250	251.1	0.069
500	105.8	0.030

60Å



250Å



Protein Adsorption

- Silica has strong –ve charge above pH 3.5
- Proteins have +ve below pI
- Adsorption coefficient (K) indicates the strength of the interaction: higher = stronger interaction
- The strength of the interaction correlates to the rate of release

BioSilicon Technology

Potential for The Future of Protein Delivery